

10/780297

Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
BRS	L1	11466	erythropoietin	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:06			
BRS	L2	8919	composition same buffer same (sulfate or citrate or phosphate) same pH	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:06			
BRS	L3	9	erythropoietin same (composition same buffer same (sulfate or citrate or phosphate) same pH)	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:07			
BRS	L4	581	glycosylat\$3 same erythropoietin	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:07			
BRS	L5	83	(peg same erythropoietin same conjugat\$3) or (pegylated adj erythropoietin)	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:08			
BRS	L6	66	(pegylat\$3 same erythropoietin)	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:08			
BRS	L7	1671	(erythropoietin same (modif\$7 or substitut\$3 or mutat\$3)) or (glycosylat\$3 same erythropoietin) or ((peg same erythropoietin same conjugat\$3) or (pegylated adj erythropoietin)) or ((pegylat\$3 same erythropoietin))	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:08			

Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
			(composition same buffer same (sulfate or citrate or phosphate) same pH) same ((erythropoietin same (modi\$7 or substitut\$3 or mutat\$3)) or (glycosylat\$3 same erythropoietin) or ((peg same erythropoietin same conjugat\$3) or (pegylated adj erythropoietin)) or ((pegylat\$3 same erythropoietin)))	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:09			
8	BRS	L8	1					
9	BRS	L9	172131	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:09			
10	BRS	L10	86037	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:10			
11	BRS	L11	177257	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:10			
12	BRS	L12	6	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:10			
13	BRS	L13	1443	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:11			
14	BRS	L14	5674	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:12			

Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
			((erythropoietin same (composition same buffer same (sulfate or citrate or phosphate) same pH)) same ((sodium adj chloride) or isotonic\$5) or (methionine or arginine) or (polyol or mannitol))) same ((pluronic adj f68) or poloxamer)	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:12			
15 BRS	L15	0						
16 BRS	L16	749	multiply adj charged	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:12			
17 BRS	L17	303	multiple adj charged	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:12			
18 BRS	L18	17	papadimitriou adj apollon.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:13			
19 BRS	L19	7	erythropoietin and (papadimitriou adj apollon.in.)	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:13			
20 BRS	L20	5	erythropoietin and (papadimitriou adj apollon.in.) and (composition same buffer same (sulfate or citrate or phosphate) same pH)	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:13			
21 BRS	L21	92	((multiply adj charged) or (multiple adj charged)) same anion	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:14			
22 BRS	L22	4	composition same buffer same ((multiply adj charged) or (multiple adj charged)) same anion) same pH	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:14			
23 BRS	L23	182	((pegylated or peg) same erythropoietin	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:14			
24 BRS	L24	301588	linker or linking	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:14			

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
25	BRS	L25	36685	kilodalton or kDa	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:15			
26	BRS	L26	2	(((pegylated or peg) same erythropoietin) same (linker or linking)) same (kilodalton or kDa)	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:15			
27	BRS	L27	20	(((pegylated or peg) same erythropoietin) same (linker or linking)	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:15			
28	BRS	L28	0	composition same sulfate same arinine same pH	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:16			
29	BRS	L29	0	composition same sulfate same arinine same pH	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:16			
30	BRS	L30	0	erythropoietin same (composition same sulfate same arinine same pH)	US-PGPUB; USPAT; EPO; JPO; DERWENT	2004/12/03 08:16			

=> d his

(FILE 'HOME' ENTERED AT 08:18:56 ON 03 DEC 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA'
ENTERED AT

08:19:22 ON 03 DEC 2004

L1 79889 S ERYTHROPOIETIN
L2 6670 S COMPOSITION (P) BUFFER (P) (SULFATE OR CITRATE OR
PHOSPHATE)
L3 10 S L1 (P) L2
L4 10 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)
L5 780 S GLYCOSYLAT? (P) L1
L6 22 S PEG (P)L1 (P) (CONJUGAT? OR COVALENT?)
L7 81 S PEGYLAT? (P) L1
L8 3892 S L1 (P) (MODIF? OR SUBSTITUT? OR MUTAT?)
L9 4625 S L5 OR L6 OR L7 OR L8
L10 0 S L2 (P) L9
L11 298406 S (SODIUM CHLORIDE) OR ISOTON?
L12 572259 S METHIONINE OR ARGININE
L13 142861 S POLYOL OR MANNITOL
L14 1 S L4 (P) (L12 OR L11 OR L13)
L15 1255 S PLURONIC F68
L16 5705 S POLOXAMER
L17 1 S L14 AND (L15 OR L16)
L18 482 S PAPADIMITRIOU A?/AU
L19 7 S L18 AND L1
L20 3 DUPLICATE REMOVE L19 (4 DUPLICATES REMOVED)
L21 1864732 S LINK?
L22 566 S L9 (P) L21
L23 0 S L22 AND L2

=> log y

FILE 'MEDLINE' ENTERED AT 08:19:22 ON 03 DEC 2004

FILE 'CAPLUS' ENTERED AT 08:19:22 ON 03 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE 'EMBASE' ENTERED AT 08:19:22 ON 03 DEC 2004
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FILE 'SCISEARCH' ENTERED AT 08:19:22 ON 03 DEC 2004
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FILE 'AGRICOLA' ENTERED AT 08:19:22 ON 03 DEC 2004

=> s erythropoietin
L1 79889 ERYTHROPOIETIN

=> s composition (p) buffer (p) (sulfate or citrate or phosphate)
L2 6670 COMPOSITION (P) BUFFER (P) (SULFATE OR CITRATE OR PHOSPHATE)

=> s l1 (p) l2
L3 10 L1 (P) L2

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'CAPLUS, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L3
L4 10 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

=> 'd l4 1-10 ibib abs
'D IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d l4 1-10 ibib abs

L4 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:355193 CAPLUS
DOCUMENT NUMBER: 140:363055
TITLE: Microencapsulation and sustained release of
biologically active polypeptides
INVENTOR(S): Costantino, Henry R.; Hotz, Joyce
PATENT ASSIGNEE(S): Alkermes Controlled Therapeutics, Inc. II, USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004036186	A2	20040429	WO 2003-US33168	20031017
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004208929	A1	20041021	US 2003-688059	20031017
US 2004228833	A1	20041118	US 2003-688786	20031017
PRIORITY APPLN. INFO.:			US 2002-419388P	P 20021017

AB This invention relates to ***compns*** . for the sustained release of biol. active polypeptides, and methods of forming and using said ***compns*** ., for the sustained release of biol. active polypeptides, such as glucagon, glucagon-like peptides, exendins, vasoactive intestinal peptide, Igs, antibodies, cytokines, interleukins, macrophage activating

factors, interferons, ***erythropoietin*** tumor necrosis factor, colony stimulating factors, hormones, etc. The sustained release ***comps*** of this invention comprise a biocompatible polymer having dispersed therein, a biol. active polypeptide, a sugar and a salting-out salt. For example, exendin-4 was encapsulated in poly(lactide-co-glycolide) using a water-oil-oil (W/O/O) emulsion system. The initial embryonic microparticles were formed in a W/O/O inner emulsion step after which they were subjected to coacervation and hardening steps. The inner phase was prep'd. by dissolving the exendin-4, sucrose and ammonium ***sulfate*** in water or an aq. ***buffer*** and injected into a polymer phase (PLG dissolved in methylene chloride) while sonicating. The resultant water/oil emulsion was then mixed with silicone oil, and the mixt. was added to heptene to form microparticles. The microparticles were collected, dried and filled into vials.

L4 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:60340 CAPLUS

DOCUMENT NUMBER: 140:117364

TITLE: Stable pharmaceutical composition of erythropoietin comprising a poloxamer polyol and a polyhydric alcohol and use for anemia therapy

INVENTOR(S): Vukmirovic, Andreja; Rozman, Tanja; Svetek, Jelka; Paris, Alenka

PATENT ASSIGNEE(S): Lek Pharmaceuticals D.D., Slovenia

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006958	A1	20040122	WO 2003-SI23	20030714

W: AT, AU, BA, BG, BR, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, HR, HU, ID, IL, IN, JP, KR, LT, LU, LV, MK, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SK, TR, UA, US, ZA

RW: BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

SI 21258	C	20040229	SI 2002-178	20020717
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PRIORITY APPLN. INFO.:	SI 2002-178	A	20020717
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AB The present invention provides a new stable pharmaceutical compn. of erythropoietin (EPO) that is stabilized with a combination of a poloxamer polyol and a polyhydric alc. The stabilization of EPO is achieved while the compn. of the invention is preferably free of additives which are derived from human or animal origin other than EPO (e.g. serum proteins). The pharmaceutical compn. optionally further comprises an isotonifying agent and/or one or more pharmaceutically acceptable excipients. The pharmaceutical compn. of the present invention is suitable for use in human and veterinary medicine and is pharmaceutically acceptable in a suitable administration form, esp. for parenteral application, e.g. i.m., s.c. and/or i.v. application. In a particularly preferred embodiment, the pharmaceutical compn. of the present invention is in a liq., more preferably in an aq. form.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:60332 CAPLUS

DOCUMENT NUMBER: 140:117404

TITLE: Stable pharmaceutical composition comprising erythropoietin

INVENTOR(S): Vukmirovic, Andreja; Rozman, Tanja; Svetek, Jelka; Paris, Alenka

PATENT ASSIGNEE(S): Lek Pharmaceuticals D.D., Slovenia

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006948	A1	20040122	WO 2002-IB4690	20021108

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
 CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

SI 21257 C 20040229 SI 2002-176 20020717

PRIORITY APPLN. INFO.: SI 2002-176 A 20020717

AB The present invention provides a new stable pharmaceutical ***comprn***
 . of ***erythropoietin*** (EPO) that is stabilized with PVP. Stable
 comprns . contained ***erythropoietin*** , PVP K12, NaCl and
 phosphate ***buffer*** .

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
 STN

ACCESSION NUMBER: 2004:7415 BIOSIS
 DOCUMENT NUMBER: PREV200400008350
 TITLE: Erythropoietin liposomal dispersion.
 AUTHOR(S): Naeff, Rainer [Inventor, Reprint Author]; Delmenico, Sandro
 [Inventor]; Wetter, Andre [Inventor]; Floether,
 Frank-Ulrich [Inventor]
 CORPORATE SOURCE: Langwiesen, Switzerland
 ASSIGNEE: Cilag AG, Switzerland
 PATENT INFORMATION: US 6645522 November 11, 2003
 SOURCE: Official Gazette of the United States Patent and Trademark
 Office Patents, (Nov 11 2003) Vol. 1276, No. 2.
<http://www.uspto.gov/web/menu/patdata.html>. e-file.
 ISSN: 0098-1133 (ISSN print).
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 ENTRY DATE: Entered STN: 17 Dec 2003
 Last Updated on STN: 17 Dec 2003

AB The present invention relates to a liposome based formulation of
 erythropoietin comprising: (a) an effective amount of an
 erythropoietin ; (b) a lipidic phase comprising: (i) lecithin or
 hydrogenated lecithin; (ii) optionally, a charged electropositive or
 electronegative lipid compound; and (iii) cholesterol or a derivative
 thereof selected from cholesterol esters, polyethylene glycol derivatives
 of cholesterol (PEG-cholesterols), and organic acid derivatives of
 cholesterols; and (c) a ***phosphate*** ***buffer*** . The
 liposome based parenteral dosage form of the invention is prepared by
 means of an ethanol injection technique. The ***composition*** avoids
 the need for use of human serum albumin and exhibits superior stability.

L4 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:850963 CAPLUS
 DOCUMENT NUMBER: 136:11065
 TITLE: New pharmaceutical composition
 INVENTOR(S): Papadimitriou, Apollon
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
 SOURCE: PCT Int. Appl., 64 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087329	A1	20011122	WO 2001-EP5187	20010508
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, DE, DK, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2408685	AA	20011122	CA 2001-2408685	20010508
BR 2001010914	A	20030211	BR 2001-10914	20010508
EP 1311285	A2	20030521	EP 2001-943331	20010508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 JP 2003533487 T2 20031111 JP 2001-583796 20010508
 US 2002037841 A1 20020328 US 2001-853731 20010511
 ZA 2002008500 A 20040128 ZA 2002-8500 20021021
 NO 2002005450 A 20021114 NO 2002-5450 20021114
 US 2004147431 A1 20040729 US 2004-780297 20040217
 PRIORITY APPLN. INFO.: EP 2000-110355 A 20000515
 WO 2001-EP5187 W 20010508
 US 2001-853731 A1 20010511

AB The present invention relates to a liq. pharmaceutical compn. comprising an erythropoietin protein, a multiple charged inorg. anion in a pharmaceutically acceptable buffer suitable to keep the soln. pH in the range from about 5.5 to about 7.0, and optionally one or more pharmaceutically acceptable excipients. This compn. is esp. useful for the prophylaxis and treatment of diseases related to erythropoiesis.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:197980 CAPLUS
 DOCUMENT NUMBER: 132:227484
 TITLE: Aqueous formulations of biologically active polypeptides
 INVENTOR(S): Papadimitriou, Apollon
 PATENT ASSIGNEE(S): Hoffmann-La Roche, A.-G., Switz.
 SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000086532	A2	20000328	JP 1999-248013	19990901
TW 570805	B	20040111	TW 1999-88114073	19990818
EP 1002547	A1	20000524	EP 1999-116537	19990824
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1250669	A	20000419	CN 1999-119245	19990827
NZ 337527	A	20001222	NZ 1999-337527	19990827
SG 85670	A1	20020115	SG 1999-4209	19990827
KR 2000022777	A	20000425	KR 1999-36053	19990828
NO 9904214	A	20000302	NO 1999-4214	19990831
AU 9944866	A1	20000316	AU 1999-44866	19990831
AU 755930	B2	20030102		
TR 9902103	A2	20000421	TR 1999-9902103	19990831
HR 990272	A1	20000630	HR 1999-990272	19990831
ZA 9905601	A	20000927	ZA 1999-5601	19990831
MX 9908037	A	20000930	MX 1999-8037	19990831
RU 2180855	C2	20020327	RU 1999-118890	19990831
BR 9903984	A	20010313	BR 1999-3984	19990901
US 2002028766	A1	20020307	US 2001-953721	20010917
PRIORITY APPLN. INFO.: EP 1998-116494 A 19980901				
US 1999-385404 A3 19990830				

AB This invention relates to drug delivery systems of polypeptides with improved soly. Pharmacol. active polypeptides selected from the group consisting of hedgehog proteins, osteogenic factors, growth factors, ***erythropoietin***, thrombopoietin, G-CSF, interleukins, and interferons, are combined with amphipathic substances to form ionic complexes in formulating aq. ***comps***. .alpha.-Interferon in Tris ***buffer*** (pH 7.4) was dialyzed in a soln. contg. deoxycholic acid and phosphatidylserine and formulated with a soln. contg. NaCl, Na ***phosphate*** ***buffer*** soln. and deoxycholic acid for injection.

L4 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:549135 CAPLUS
 DOCUMENT NUMBER: 131:161653
 TITLE: Erythropoietin liposomal dispersion
 INVENTOR(S): Naff, Rainer; Delmenico, Sandro; Wetter, Andre; Flother, Frank-Ulrich
 PATENT ASSIGNEE(S): Cilag A.-G. International, Switz.
 SOURCE: PCT Int. Appl., 23 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9942085	A1	19990826	WO 1999-IB249	19990212
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 937456	A1	19990825	EP 1998-103111	19980223
EP 937456	B1	20040721		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 271376	E	20040815	AT 1998-103111	19980223
CA 2320072	AA	19990826	CA 1999-2320072	19990212
AU 9921808	A1	19990906	AU 1999-21808	19990212
AU 750481	B2	20020718		
BR 9908202	A	20001024	BR 1999-8202	19990212
JP 2002503685	T2	20020205	JP 2000-532102	19990212
NZ 506429	A	20030328	NZ 1999-506429	19990212
RU 2218914	C2	20031220	RU 2000-124317	19990212
SK 284036	B6	20040803	SK 2000-1222	19990212
US 2002028236	A1	20020307	US 1999-252563	19990218
US 6645522	B2	20031111		
NO 2000004186	A	20000822	NO 2000-4186	20000822
US 2004052838	A1	20040318	US 2003-659097	20030910
PRIORITY APPLN. INFO.:			EP 1998-103111	A 19980223
			WO 1999-IB249	W 19990212
			US 1999-252563	A1 19990218

AB The present invention relates to a liposome-based formulation of ***erythropoietin*** comprising: (a) an effective amt. of an ***erythropoietin***; (b) a lipidic phase contg. (1) lecithin or hydrogenated lecithin, (2) optionally, a charged electropos. or electroneg. lipid compd., and (3) cholesterol or a deriv. thereof selected from cholesterol esters, polyethylene glycol derivs. of cholesterol (PEG-cholesterols) and org. acid derivs. of cholesterol; and (c) a ***phosphate*** ***buffer***. The liposome-based parenteral dosage form of the invention is prepd. by means of an ethanol injection technique. The ***comprn*** avoids the need for use of human serum albumin and exhibits superior stability. A liposome-based dispersion contained ***erythropoietin*** 1 million IU, hydrogenated soya lecithin 0.5, cholesterol 0.1, Na dipalmitoylphosphatidic acid 0.04, ethanol 0.5, NaH₂PO₄.cntdot.2H₂O 0.1164, Na₂HPO₄.cntdot.2H₂O 0.2225, NaCl 0.584, and purified water to 97.9371 g.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:78461 CAPLUS
DOCUMENT NUMBER: 130:144219
TITLE: Water-in-oil microemulsions containing cholesterol
INVENTOR(S): Takahashi, Masao; Nakamura, Kaoru; Matsushita, Hiroshi
PATENT ASSIGNEE(S): Advanced Skin Research Kenkyusho K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11029464	A2	19990202	JP 1997-181237	19970707
PRIORITY APPLN. INFO.:			JP 1997-181237	19970707

AB Water-in-oil microemulsions contain oils, surfactants mainly contg. oligomeric surfactants, cholesterol, and H₂O. The microemulsions are esp. useful for carrying peptide pharmaceuticals or water-sol. and nonabsorbable low-mol.-wt. compds. A microemulsion was formed from a ***comprn*** contg. cholesterol 0.06, polyoxyethylene (10 mol ethylene oxide) hydrogenated castor oil 9.94, ***phosphate*** ***buffer*** 5.5, ***erythropoietin*** 0.0001, and iso-Pr palmitate to 100 wt.%.

L4 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1997:660651 CAPLUS
 DOCUMENT NUMBER: 127:298769
 TITLE: Composition for sustained release of non-aggregated erythropoietin
 INVENTOR(S): Zale, Stephen E.; Burke, Paul A.; Bernstein, Howard; Brickner, Avram
 PATENT ASSIGNEE(S): Alkermes, Inc., USA
 SOURCE: U.S., 15 pp., Cont.-in-part of U.S. Ser. No. 885,307, abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 13
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5674534	A	19971007	US 1995-483318	19950607
PT 644771	T	20021231	PT 1993-916466	19930609
ES 2181691	T3	20030301	ES 1993-916466	19930609
CA 2223583	AA	19961219	CA 1996-2223583	19960604
WO 9640074	A2	19961219	WO 1996-US8526	19960604
WO 9640074	A3	19970206		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
AU 9660341	A1	19961230	AU 1996-60341	19960604
AU 705968	B2	19990603		
EP 831786	A2	19980401	EP 1996-917966	19960604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001515457	T2	20010918	JP 1997-501097	19960604
US 6514533	B1	20030204	US 1997-934830	19970922
AU 9742755	A1	19980115	AU 1997-42755	19971021
AU 698016	B2	19981022		
US 2003133979	A1	20030717	US 2002-278739	20021022

PRIORITY APPLN. INFO.:

US 1992-885307	B2	19920611
US 1992-984323	B2	19921202
US 1994-279784	A2	19940725
US 1995-473544	A	19950607
US 1995-477725	A	19950607
US 1995-478502	A	19950607
US 1995-483318	A	19950607
WO 1995-US7348	W	19950607
US 1995-521744	A	19950831
WO 1996-US8526	W	19960604
US 1997-765558	A2	19970307
US 1997-934830	A1	19970922

AB A ***compn*** ., and methods of forming and using said ***compn*** ., for the sustained release of non-aggregated, biol. active, ***erythropoietin*** (EPO). The sustained release ***compn*** . of this invention comprises a polymeric matrix of a biocompatible polymer and particles of biol. active, aggregation-stabilized EPO, wherein said particles are dispersed within the biocompatible polymer. The method of the invention for producing a ***compn*** . for the sustained release of biol. active EPO, includes dissolving a biocompatible polymer in a polymer solvent to form a polymer soln., dispersing particles of biol. active, aggregation-stabilized EPO in the polymer soln., and then solidifying the polymer to form a polymeric matrix contg. a dispersion of said EPO particles. The method for using a ***compn*** . of the invention is a method for providing a therapeutically effective blood level of biol. active, non-aggregated ***erythropoietin*** in a subject for a sustained period. In this method, a subject is administered an ED of the sustained release ***compn*** . of the present invention. One example ***compn*** . contained EPO 10.0, ammonium ***sulfate*** 66.8, ***phosphate*** ***buffer*** with 5mM ***citrate*** 22.1 and inulin 1.1%.

L4 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1997:119179 CAPLUS
 DOCUMENT NUMBER: 126:135628
 TITLE: Composition for sustained release of nonaggregated erythropoietin

INVENTOR(S): Zale, Stephen E.; Burke, Paul A.; Bernstein, Howard;
 Brickner, Avram
 PATENT ASSIGNEE(S): Alkermes Controlled Therapeutics, Inc., USA
 SOURCE: PCT Int. Appl., 39 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 13
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640073	A2	19961219	WO 1996-US8474	19960603
WO 9640073	A3	19970123		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 5716644	A	19980210	US 1995-478502	19950607
AU 9659724	A1	19961230	AU 1996-59724	19960603
AU 705451	B2	19990520		
EP 871433	A2	19981021	EP 1996-917028	19960603
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11506764	T2	19990615	JP 1996-501068	19960603
PRIORITY APPLN. INFO.:				
			US 1995-478502	A 19950607
			US 1992-885307	B2 19920611
			WO 1996-US8474	W 19960603

AB A ***compn*** ., and methods of forming and using the ***compn*** ., for the sustained release of non-aggregated, biol. active ***erythropoietin*** (EPO) are described. The sustained-release ***compn*** comprises a polymeric matrix of a biocompatible polymer and particles of biol. active, aggregation-stabilized EPO, wherein the particles are dispersed within the biocompatible polymer. The ***compn*** for the sustained release of EPO is produced by dissolving the biocompatible polymer in a polymer solvent to form a polymer soln., dispersing particles of biol. active, aggregation-stabilized EPO in the polymer soln., and then solidifying the polymer to form a polymeric matrix contg. a dispersion of the EPO particles. Thus, a formulation contained ***erythropoietin*** 10.0, ammonium ***sulfate*** 66.8, pH 7.5 mM ***citrate*** / ***phosphate*** ***buffer*** 22.1 and inulin 1.1%. Microspheres contg. the above aggregation-stabilized ***erythropoietin*** formulations were prepd. from polyglycolide-poly lactide. The immunoreactivity of the EPO in these microspheres was detd. by extg. the protein and analyzing by RIA.

=> s glycosylat? (p) l1
 L5 780 GLYCOSYLAT? (P) L1

=> s PEG (p) l1 (p) (conjugat? or covalent?)
 L6 22 PEG (P) L1 (P) (CONJUGAT? OR COVALENT?)

=> s pegylat? (p) l1
 L7 81 PEGYLAT? (P) L1

=> s l1 (p) (modif? or substitut? or mutat?)
 L8 3892 L1 (P) (MODIF? OR SUBSTITUT? OR MUTAT?)

=> s l5 or l6 or l7 or l8
 L9 4625 L5 OR L6 OR L7 OR L8

=> s l2 (p) l9
 L10 0 L2 (P) L9

=> s (sodium chloride) or isoton?
 L11 298406 (SODIUM CHLORIDE) OR ISOTON?

=> s methionine or arginine
 L12 572259 METHIONINE OR ARGININE

=> s polyol or mannitol
 L13 142861 POLYOL OR MANNITOL

=> s l4 (p) (l12 or l11 or l13)

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L86 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L92 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L94 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L96 (P) '
L14 1 L4 (P) (L12 OR L11 OR L13)

=> d l14 1 ibib abs

L14 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:60340 CAPLUS
DOCUMENT NUMBER: 140:117364
TITLE: Stable pharmaceutical composition of erythropoietin
comprising a poloxamer polyol and a polyhydric alcohol
and use for anemia therapy
INVENTOR(S): Vukmirovic, Andreja; Rozman, Tanja; Svetek, Jelka;
Paris, Alenka
PATENT ASSIGNEE(S): Lek Pharmaceuticals D.D., Slovenia
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006958	A1	20040122	WO 2003-SI23	20030714
W: AT, AU, BA, BG, BR, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, HR, HU, ID, IL, IN, JP, KR, LT, LU, LV, MK, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SK, TR, UA, US, ZA				
RW: BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				

SI 21258	C	20040229	SI 2002-178	20020717
PRIORITY APPLN. INFO.:			SI 2002-178	A 20020717

AB The present invention provides a new stable pharmaceutical compn. of erythropoietin (EPO) that is stabilized with a combination of a poloxamer polyol and a polyhydric alc. The stabilization of EPO is achieved while the compn. of the invention is preferably free of additives which are derived from human or animal origin other than EPO (e.g. serum proteins). The pharmaceutical compn. optionally further comprises an isotonicizing agent and/or one or more pharmaceutically acceptable excipients. The pharmaceutical compn. of the present invention is suitable for use in human and veterinary medicine and is pharmaceutically acceptable in a suitable administration form, esp. for parenteral application, e.g. i.m., s.c. and/or i.v. application. In a particularly preferred embodiment, the pharmaceutical compn. of the present invention is in a liq., more preferably in an aq. form.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s pluronic f68
L15 1255 PLURONIC F68

=> s poloxamer
L16 5705 POLOXAMER

=> s l15 and (l16 or l17)
L17 NOT FOUND

The L-number entered could not be found. To see the definition of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l14 and (l15 or l16)
L17 1 L14 AND (L15 OR L16)

=> s papadimitriou a?/au
L18 482 PAPADIMITRIOU A?/AU

=> s l18 and l1
L19 7 L18 AND L1

=> duplicate remove l19
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'

KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L19
L20 3 DUPLICATE REMOVE L19 (4 DUPLICATES REMOVED)

=> d 120 1-3 ibib abs

L20 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:850963 CAPLUS
DOCUMENT NUMBER: 136:11065
TITLE: New pharmaceutical composition
INVENTOR(S): ***Papadimitriou, Apollon***
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087329	A1	20011122	WO 2001-EP5187	20010508
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, DE, DK, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2408685	AA	20011122	CA 2001-2408685	20010508
BR 2001010914	A	20030211	BR 2001-10914	20010508
EP 1311285	A2	20030521	EP 2001-943331	20010508
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2003533487	T2	20031111	JP 2001-583796	20010508
US 2002037841	A1	20020328	US 2001-853731	20010511
ZA 2002008500	A	20040128	ZA 2002-8500	20021021
NO 2002005450	A	20021114	NO 2002-5450	20021114
US 2004147431	A1	20040729	US 2004-780297	20040217
PRIORITY APPLN. INFO.:			EP 2000-110355	A 20000515
			WO 2001-EP5187	W 20010508
			US 2001-853731	A1 20010511

AB The present invention relates to a liq. pharmaceutical compn. comprising an ***erythropoietin*** protein, a multiple charged inorg. anion in a pharmaceutically acceptable buffer suitable to keep the soln. pH in the range from about 5.5 to about 7.0, and optionally one or more pharmaceutically acceptable excipients. This compn. is esp. useful for the prophylaxis and treatment of diseases related to erythropoiesis.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:197980 CAPLUS
DOCUMENT NUMBER: 132:227484
TITLE: Aqueous formulations of biologically active polypeptides
INVENTOR(S): ***Papadimitriou, Apollon***
PATENT ASSIGNEE(S): Hoffmann-La Roche, A.-G., Switz.
SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000086532	A2	20000328	JP 1999-248013	19990901
TW 570805	B	20040111	TW 1999-88114073	19990818
EP 1002547	A1	20000524	EP 1999-116537	19990824
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
CN 1250669	A	20000419	CN 1999-119245	19990827
NZ 337527	A	20001222	NZ 1999-337527	19990827
SG 85670	A1	20020115	SG 1999-4209	19990827

KR 2000022777	A	20000425	KR 1999-36053	19990828
NO 9904214	A	20000302	NO 1999-4214	19990831
AU 9944866	A1	20000316	AU 1999-44866	19990831
AU 755930	B2	20030102		
TR 9902103	A2	20000421	TR 1999-9902103	19990831
HR 990272	A1	20000630	HR 1999-990272	19990831
ZA 9905601	A	20000927	ZA 1999-5601	19990831
MX 9908037	A	20000930	MX 1999-8037	19990831
RU 2180855	C2	20020327	RU 1999-118890	19990831
BR 9903984	A	20010313	BR 1999-3984	19990901
US 2002028766	A1	20020307	US 2001-953721	20010917
PRIORITY APPLN. INFO.:			EP 1998-116494	A 19980901
			US 1999-385404	A3 19990830

AB This invention relates to drug delivery systems of polypeptides with improved soly. Pharmacol. active polypeptides selected from the group consisting of hedgehog proteins, osteogenic factors, growth factors, ***erythropoietin***, thrombopoietin, G-CSF, interleukins, and interferons, are combined with amphipathic substances to form ionic complexes in formulating aq. compns. .alpha.-Interferon in Tris buffer (pH 7.4) was dialyzed in a soln. contg. deoxycholic acid and phosphatidylserine and formulated with a soln. contg. NaCl, Na phosphate buffer soln. and deoxycholic acid for injection.

L20 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 1
 ACCESSION NUMBER: 1998139480 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 9473251
 TITLE: Purging of mammary carcinoma cells during ex vivo culture of CD34+ hematopoietic progenitor cells with recombinant immunotoxins.
 AUTHOR: Spyridonidis A; Schmidt M; Bernhardt W; ***Papadimitriou***
 *** A*** ; Azemar M; Wels W; Groner B; Henschler R
 CORPORATE SOURCE: Department of Hematology/Oncology, University Medical Center, Freiburg, Germany.
 SOURCE: Blood, (1998 Mar 1) 91 (5) 1820-7.
 Journal code: 7603509. ISSN: 0006-4971.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
 ENTRY MONTH: 199803
 ENTRY DATE: Entered STN: 19980326
 Last Updated on STN: 20020420
 Entered Medline: 19980316

AB Tumor cells have been found in autologous hematopoietic cell transplants used after high-dose chemotherapy. To specifically eliminate contaminating mammary tumor cells during ex vivo expansion of CD34+ hematopoietic progenitor cells, we used recombinant immunotoxins (ITs) directed against cell-surface antigens expressed on mammary carcinoma cells. ITs were expressed from fusion cDNAs combining a single-chain antibody fragment (scFv) directed against the Erb-B2 or epidermal growth factor (EGF) receptors with a truncated Pseudomonas exotoxin A fragment devoid of its cell-binding domain. CD34+ hematopoietic progenitor cells did not express Erb-B2 and EGF receptors as detected by Western blotting. Ex vivo expansion of total hematopoietic cells or of colony-forming cells from CD34+ progenitors in the presence of stem-cell factor (SCF), interleukin-1 (IL-1), IL-3, IL-6, and ***erythropoietin*** (Epo) was not affected when ITs were added to the cultures. In contrast, MDA-MB 453 and MCF-7 mammary carcinoma cells were depleted in a dose- and time-dependent manner by more than 3 log in coculture with CD34+ cells over a period of 7 days in the presence of 100 to 1,000 ng/mL of anti-Erb-B2 IT. This included elimination of the subpopulations with regrowth potential. Similarly, addition of either anti-Erb-B2 or anti-EGF receptor ITs to primary breast cancer cells isolated from patients with metastatic disease resulted in elimination of cytokeratin-positive cells in seven of seven samples. ITs are highly efficient and convenient to use for the depletion of mammary tumor cells during ex vivo expansion of hematopoietic progenitor-cell autografts.

=> s link?
 L21 1864732 LINK?

=> d his

(FILE 'HOME' ENTERED AT 08:18:56 ON 03 DEC 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT

08:19:22 ON 03 DEC 2004

L1 79889 S ERYTHROPOIETIN
L2 6670 S COMPOSITION (P) BUFFER (P) (SULFATE OR CITRATE OR PHOSPHATE)
L3 10 S L1 (P) L2
L4 10 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)
L5 780 S GLYCOSYLAT? (P) L1
L6 22 S PEG (P)L1 (P) (CONJUGAT? OR COVALENT?)
L7 81 S PEGYLAT? (P) L1
L8 3892 S L1 (P) (MODIF? OR SUBSTITUT? OR MUTAT?)
L9 4625 S L5 OR L6 OR L7 OR L8
L10 0 S L2 (P) L9
L11 298406 S (SODIUM CHLORIDE) OR ISOTON?
L12 572259 S METHIONINE OR ARGININE
L13 142861 S POLYOL OR MANNITOL
L14 1 S L4 (P) (L12 OR L11 OR L13)
L15 1255 S PLURONIC F68
L16 5705 S POLOXAMER
L17 1 S L14 AND (L15 OR L16)
L18 482 S PAPADIMITRIOU A?/AU
L19 7 S L18 AND L1
L20 3 DUPLICATE REMOVE L19 (4 DUPLICATES REMOVED)
L21 1864732 S LINK?

=> s 19 (P) 124

L24 NOT FOUND

The L-number entered could not be found. To see the definition of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s 19 (p) 121

L22 566 L9 (P) L21

=> s 122 and 12

L23 0 L22 AND L2

=> d his

(FILE 'HOME' ENTERED AT 08:18:56 ON 03 DEC 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 08:19:22 ON 03 DEC 2004

L1 79889 S ERYTHROPOIETIN
L2 6670 S COMPOSITION (P) BUFFER (P) (SULFATE OR CITRATE OR PHOSPHATE)
L3 10 S L1 (P) L2
L4 10 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)
L5 780 S GLYCOSYLAT? (P) L1
L6 22 S PEG (P)L1 (P) (CONJUGAT? OR COVALENT?)
L7 81 S PEGYLAT? (P) L1
L8 3892 S L1 (P) (MODIF? OR SUBSTITUT? OR MUTAT?)
L9 4625 S L5 OR L6 OR L7 OR L8
L10 0 S L2 (P) L9
L11 298406 S (SODIUM CHLORIDE) OR ISOTON?
L12 572259 S METHIONINE OR ARGININE
L13 142861 S POLYOL OR MANNITOL
L14 1 S L4 (P) (L12 OR L11 OR L13)
L15 1255 S PLURONIC F68
L16 5705 S POLOXAMER
L17 1 S L14 AND (L15 OR L16)
L18 482 S PAPADIMITRIOU A?/AU
L19 7 S L18 AND L1
L20 3 DUPLICATE REMOVE L19 (4 DUPLICATES REMOVED)
L21 1864732 S LINK?
L22 566 S L9 (P) L21
L23 0 S L22 AND L2

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

97.69

97.90

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-8.40

-8.40

STN INTERNATIONAL LOGOFF AT 08:31:35 ON 03 DEC 2004